



PARTIAL cDNA CLONES OF THE CFTR GENE

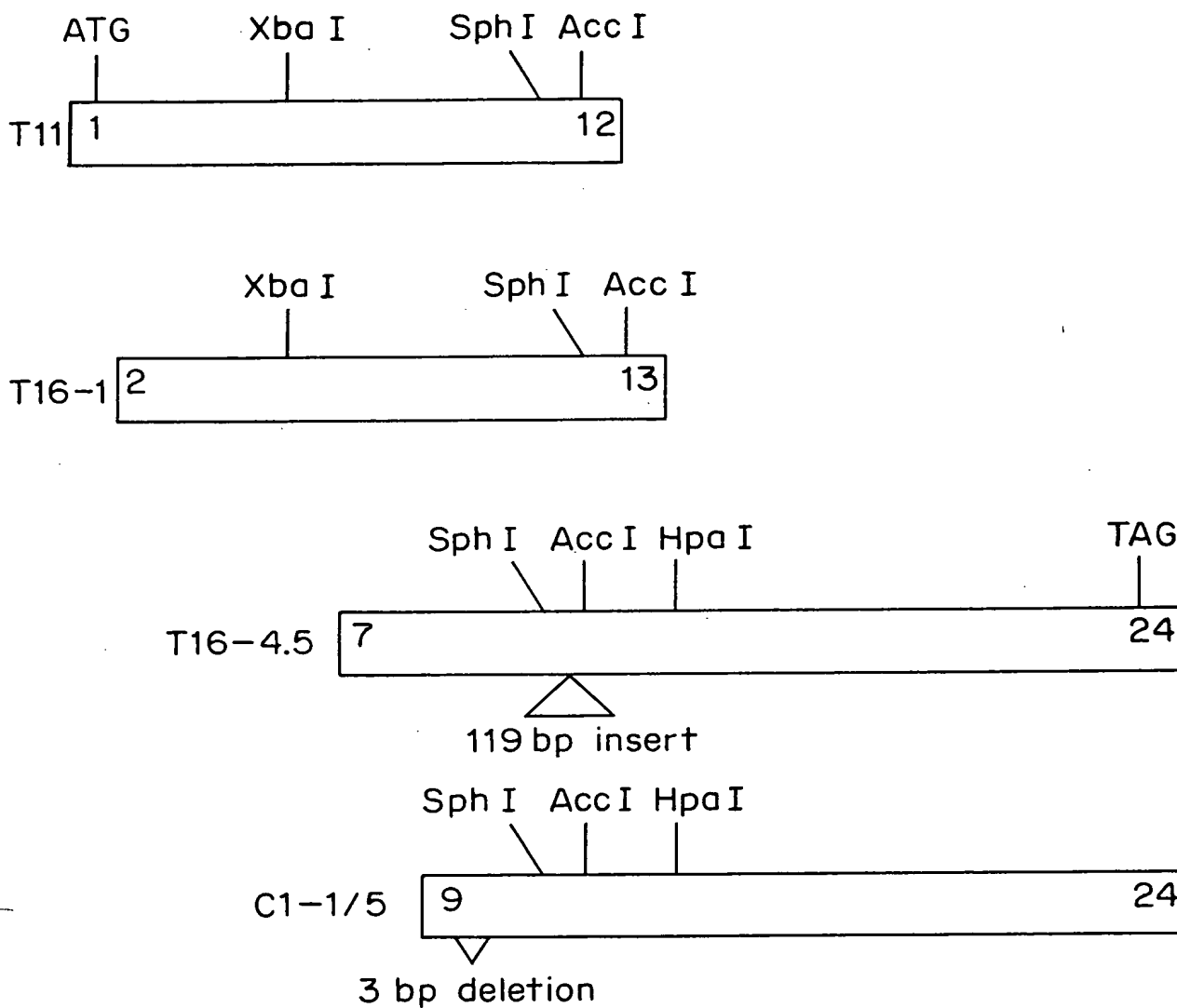


FIG. 1

STRATEGY FOR CONSTRUCTING pKK-CFTR1

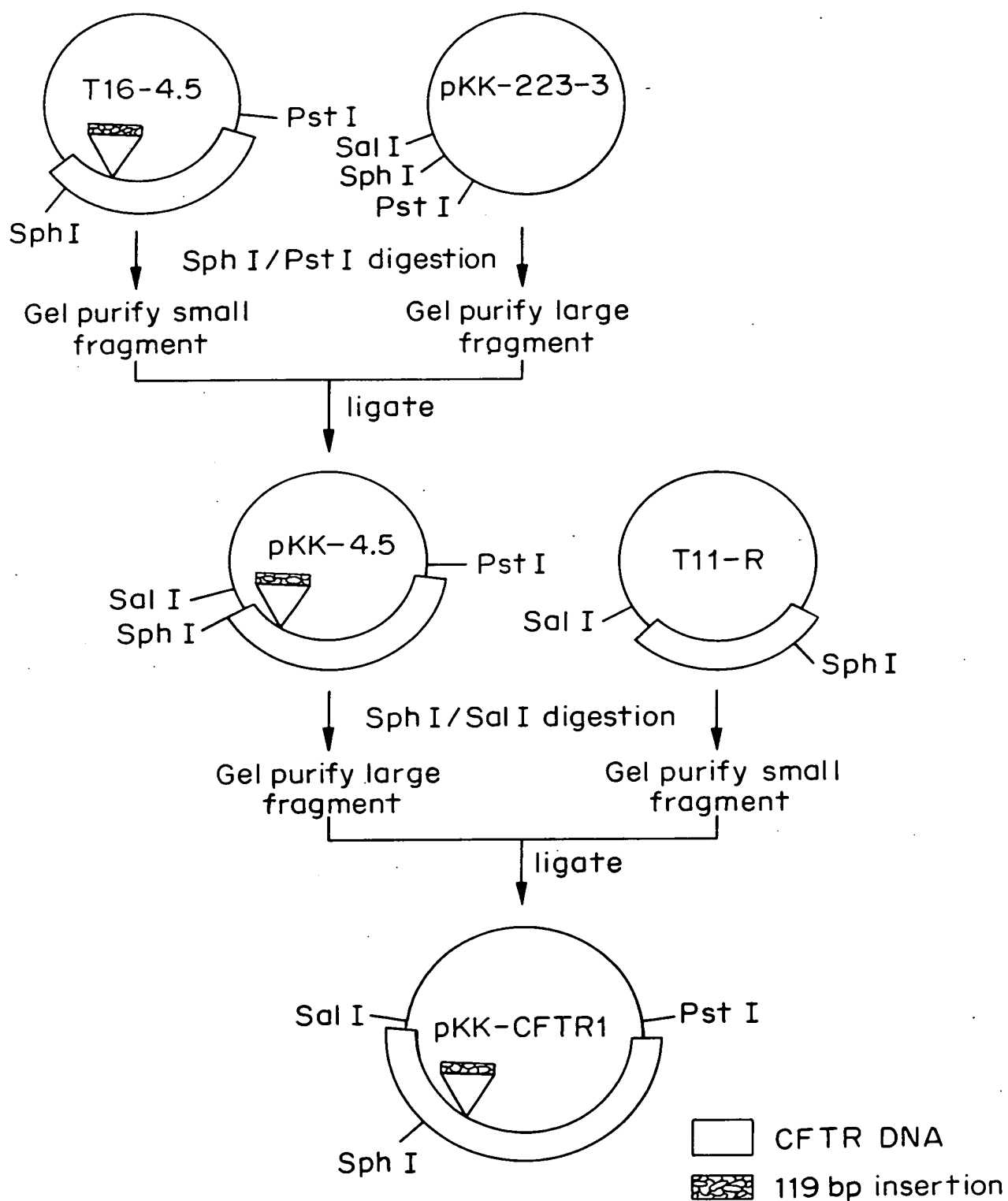


FIG. 2

CONSTRUCTION OF THE pKK-CFTR2 PLASMID

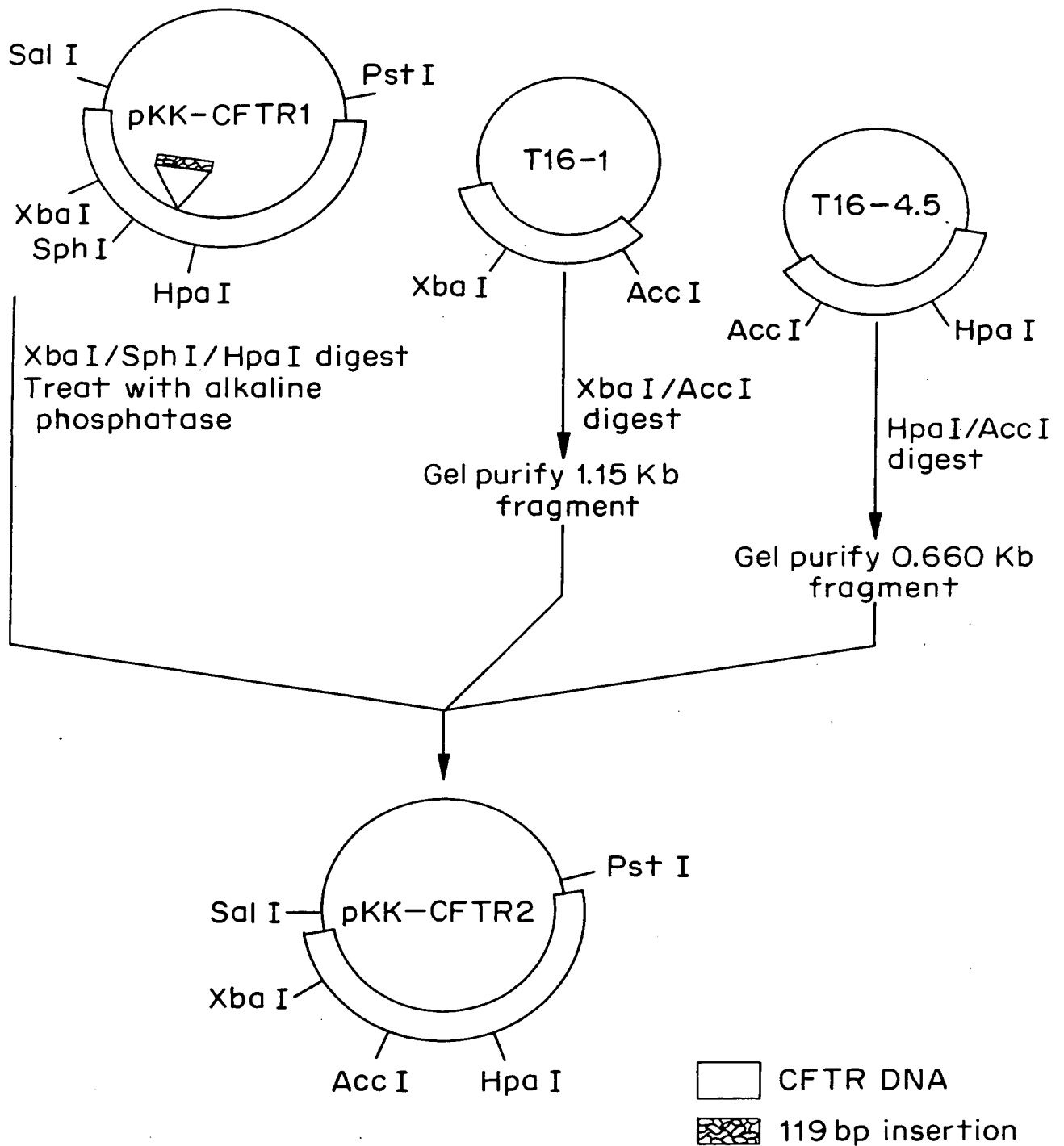


FIG. 3

STRATEGY FOR CONSTRUCTING THE pSC-CFTR2 PLASMID

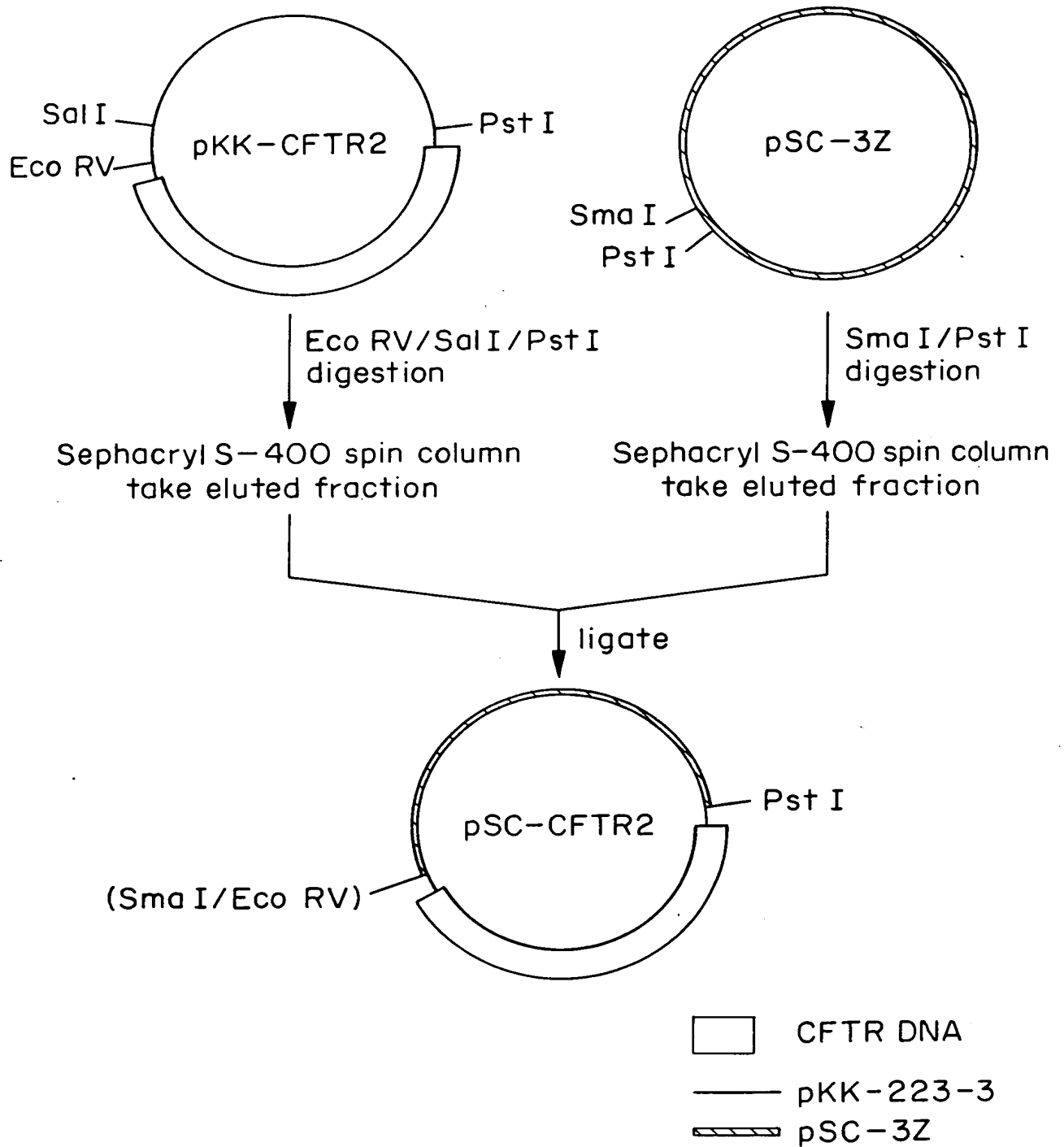


FIG. 4

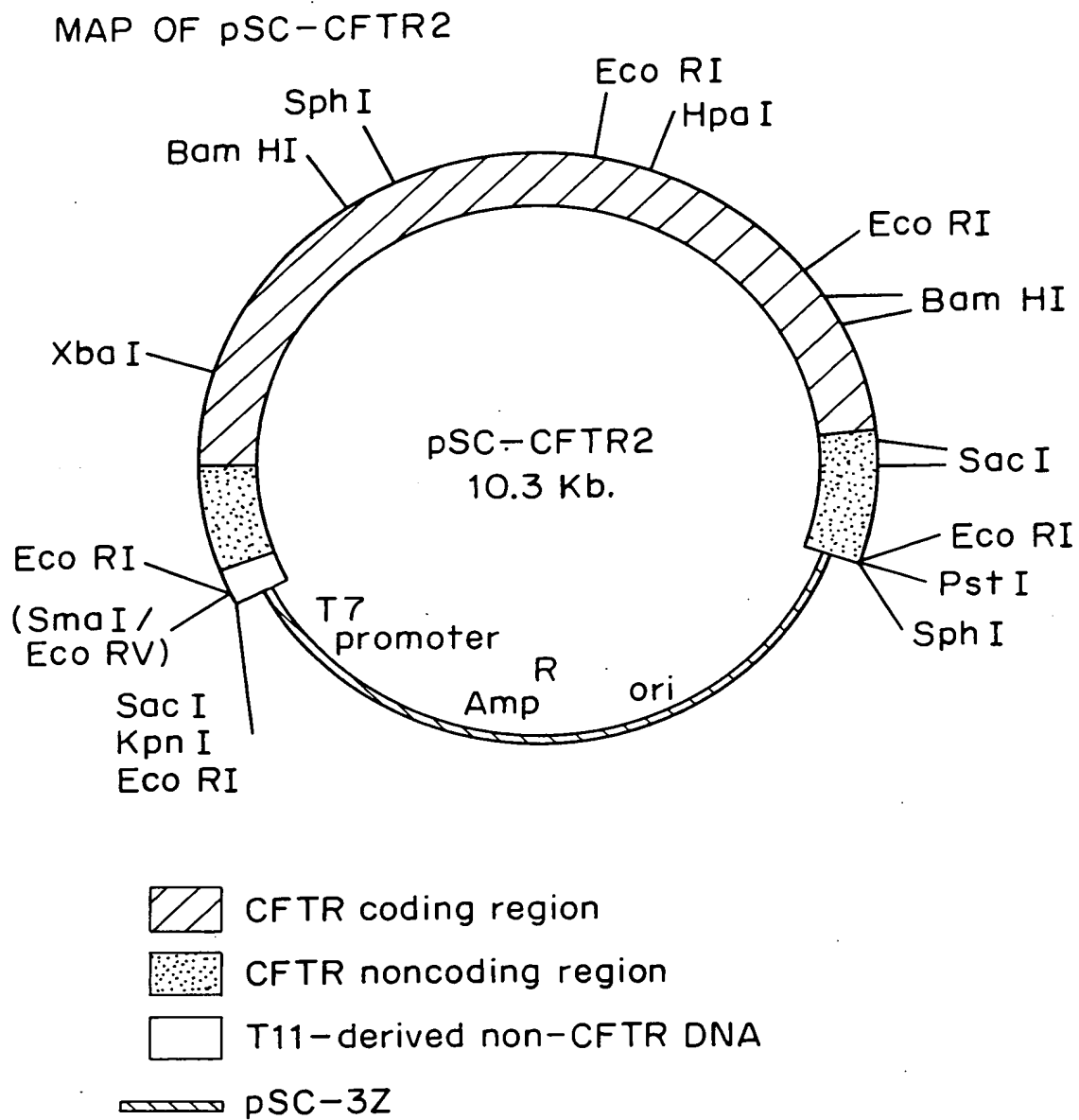


FIG. 5

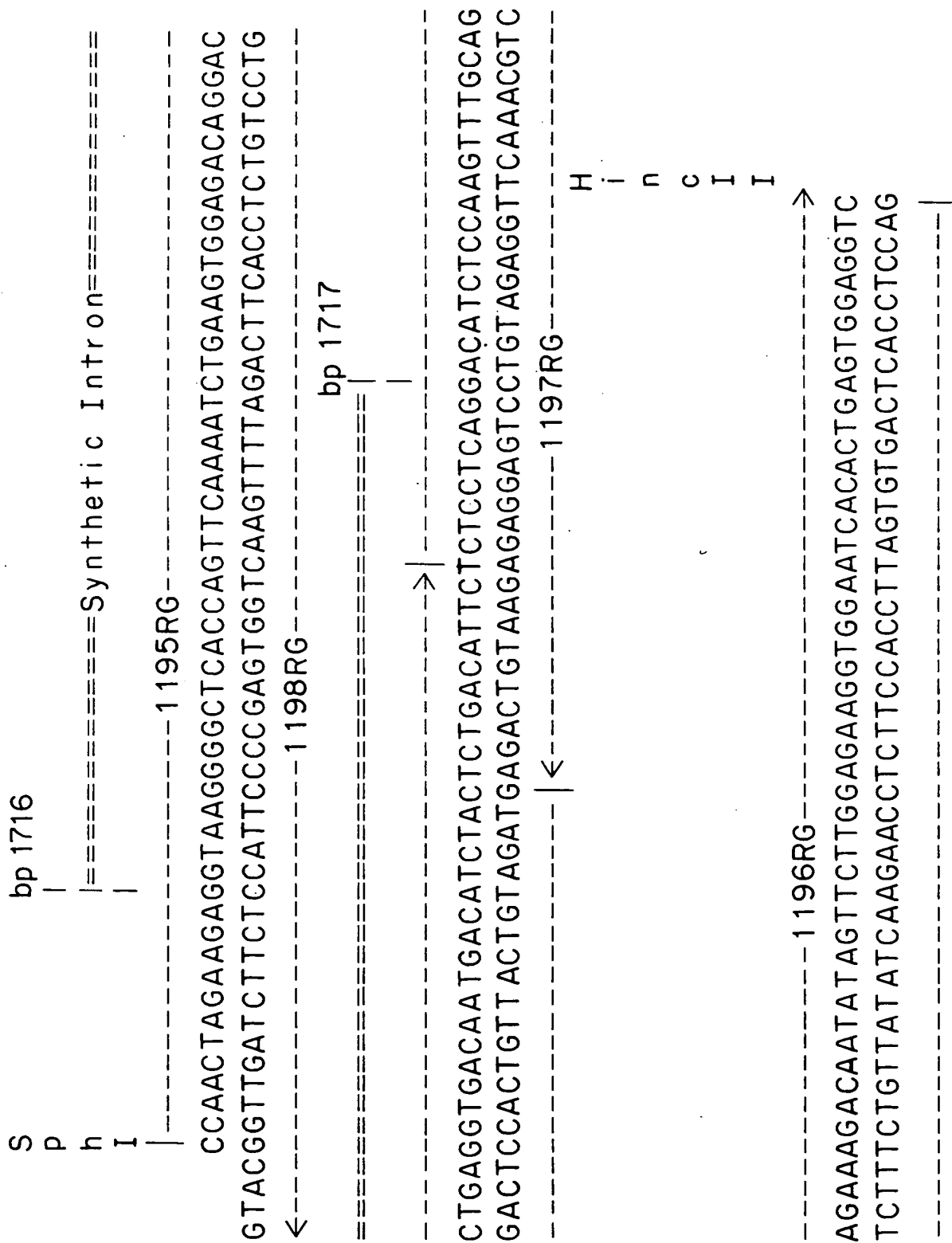


FIG. 6

CONSTRUCTION OF THE pKK-CFTR3 cDNA

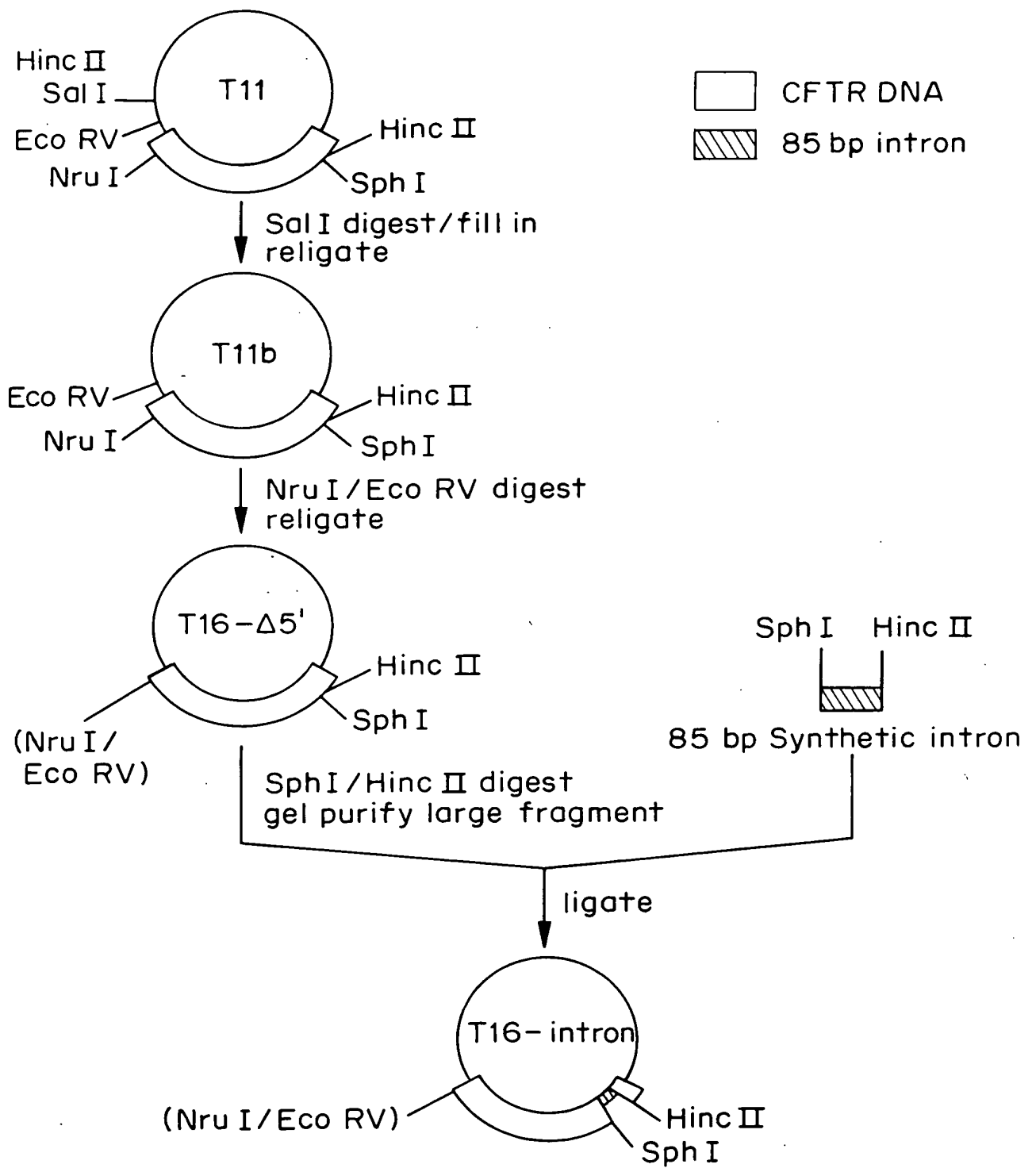


FIG. 7A

CONSTRUCTION OF THE pKK-CFTR3 CLONE (cont'd)

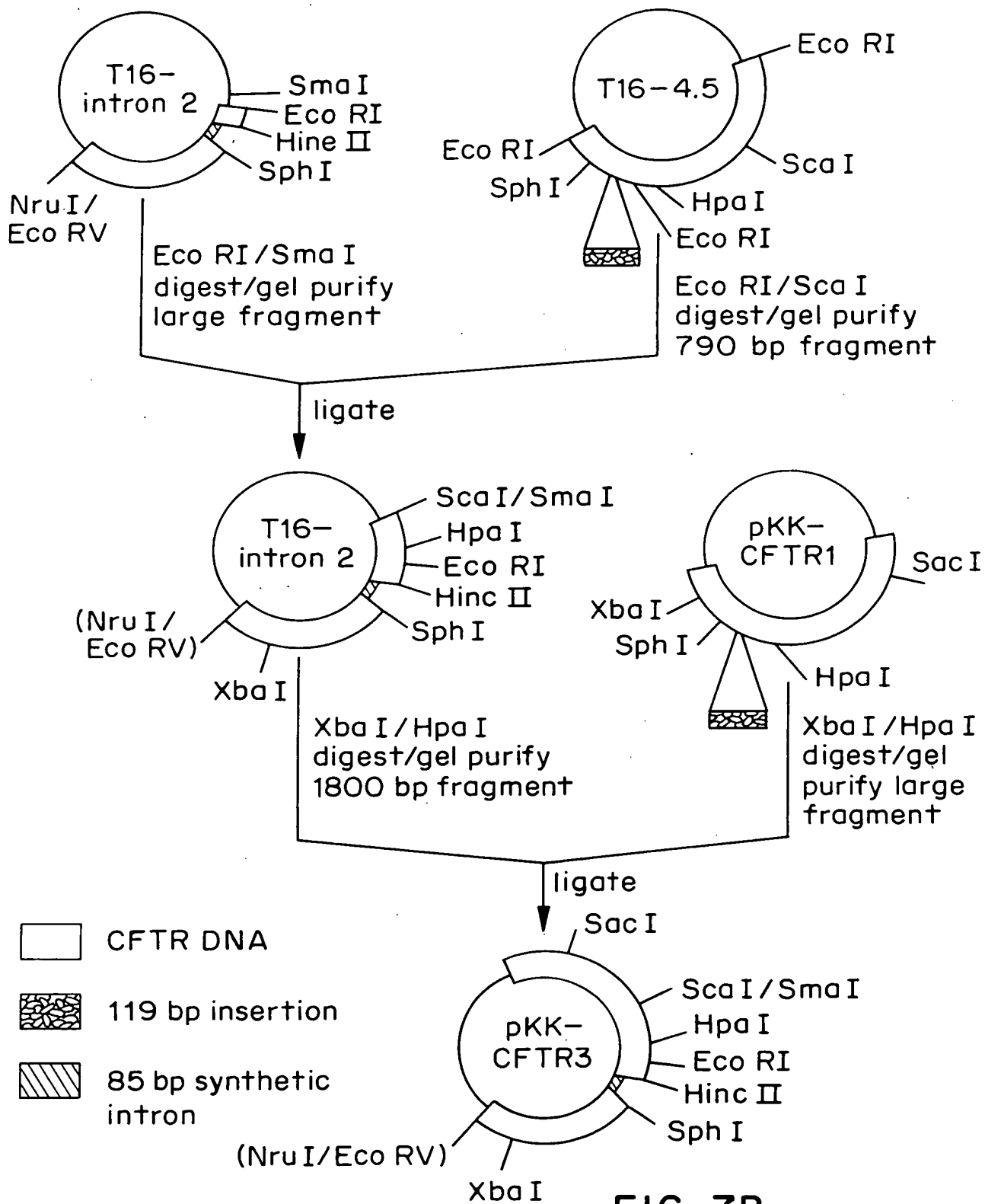
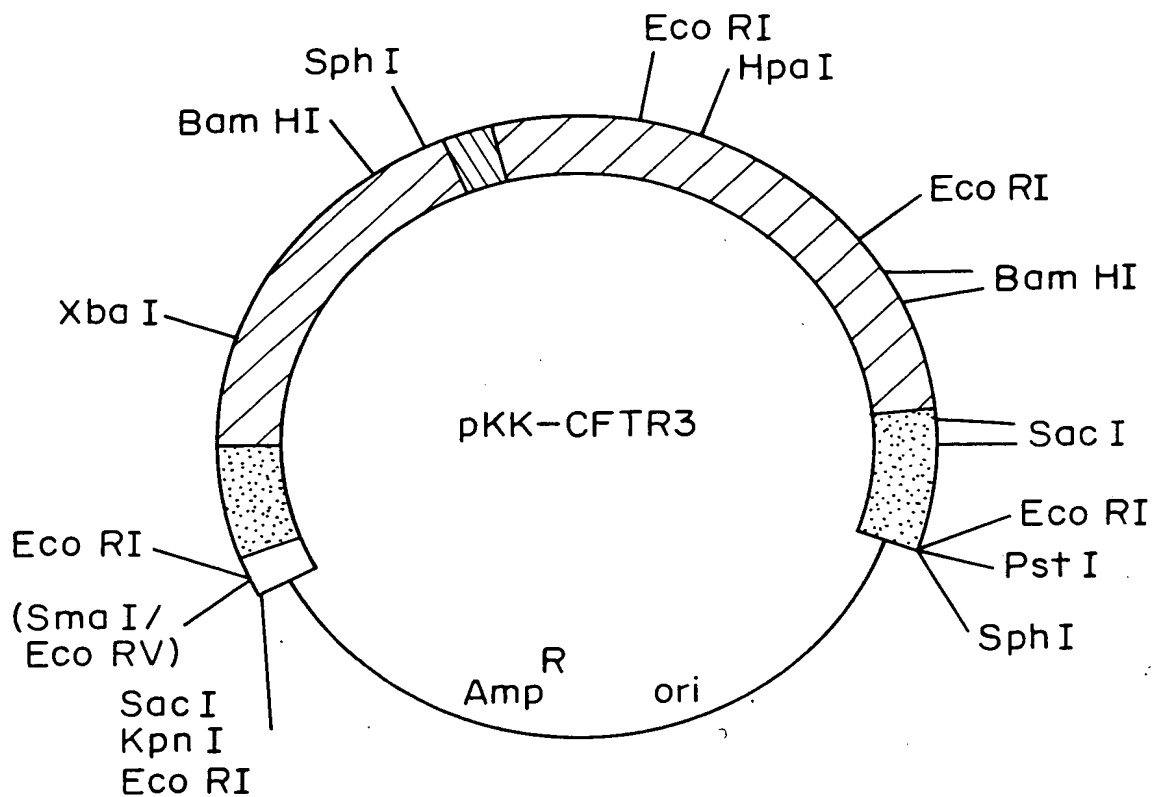


FIG. 7B

MAP OF pKK-CFTR3








-  CFTR coding region
-  CFTR noncoding region
-  85 bp intron
-  T11-derived non-CFTR DNA
-  pKK-223-3

FIG. 8

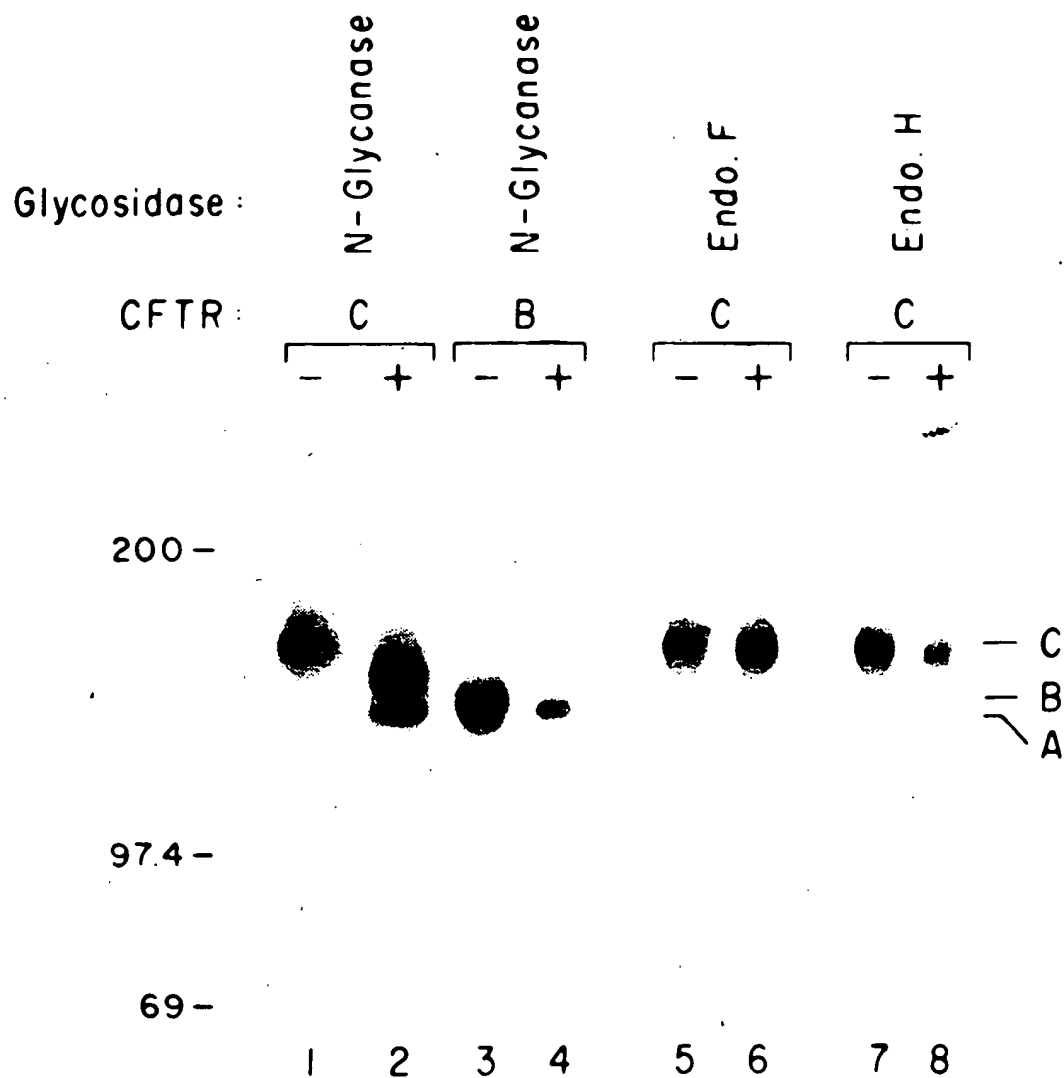


FIG.9

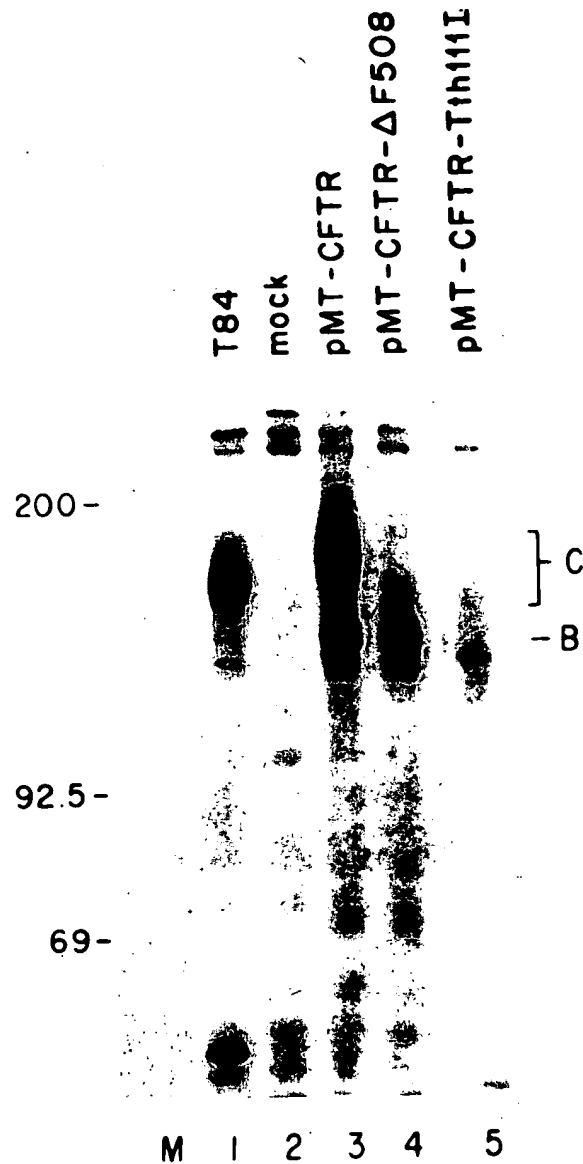


FIG.10A

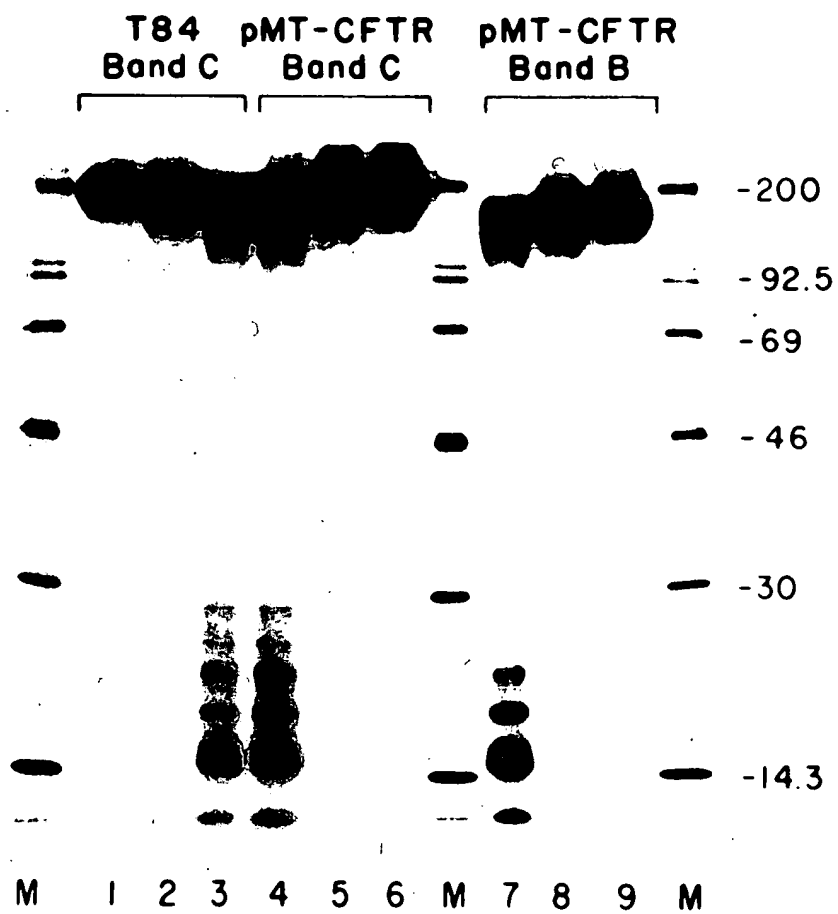


FIG.10B

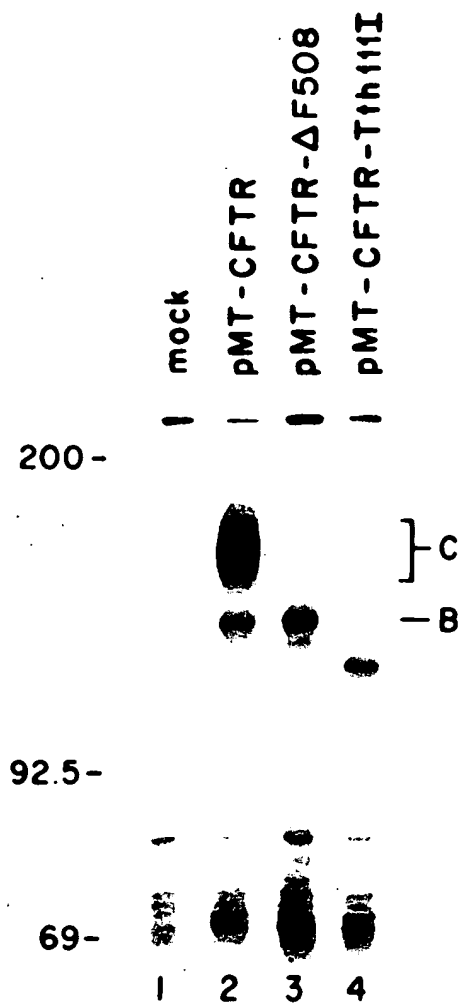


FIG.11A

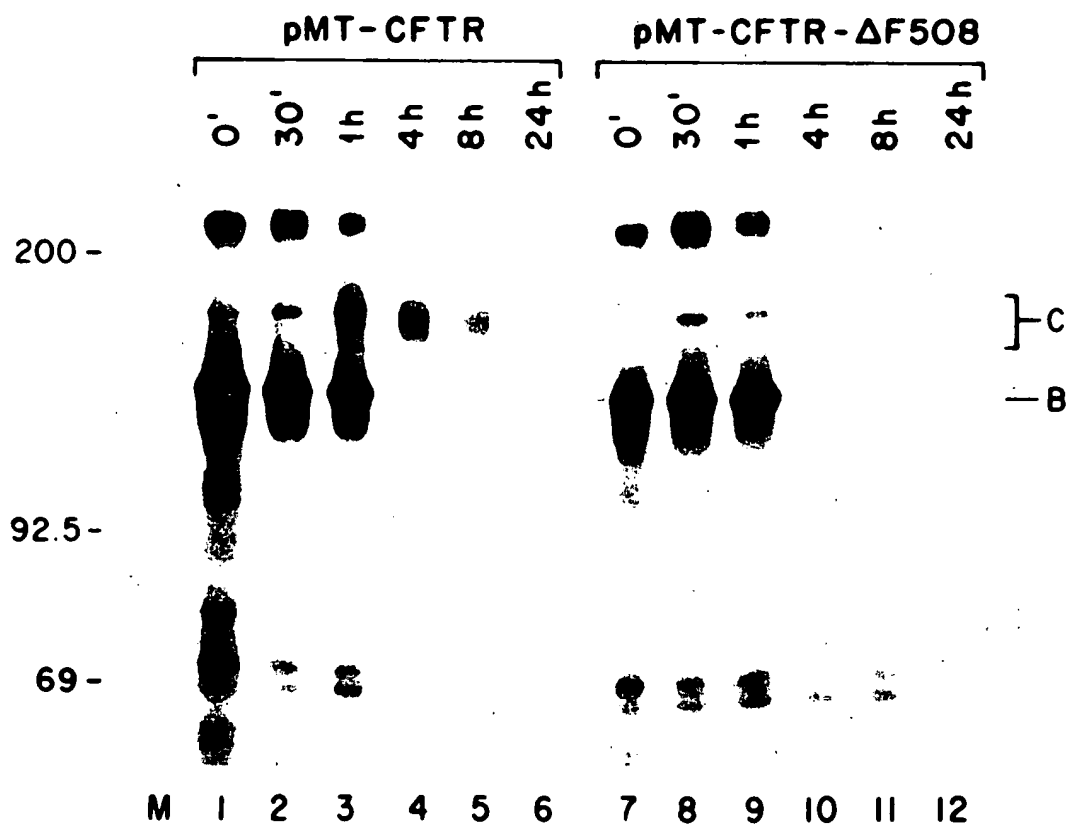


FIG.11B

FIG.12A

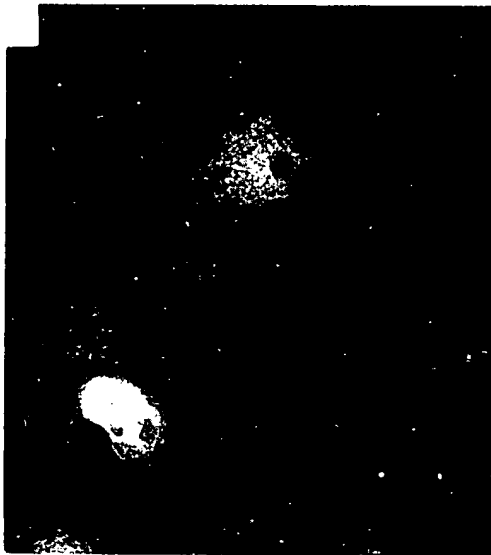


FIG.12B



FIG.12C

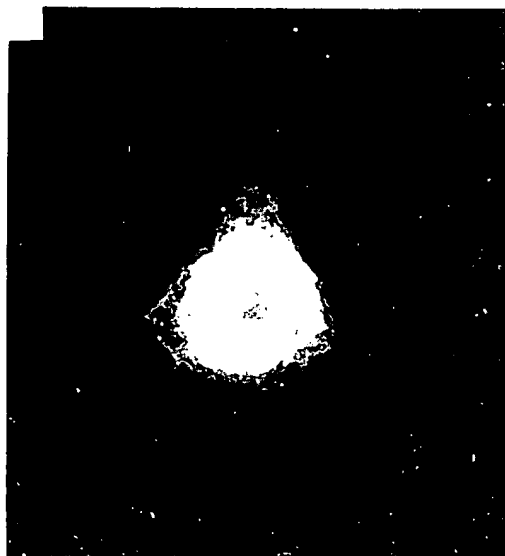


FIG.12D

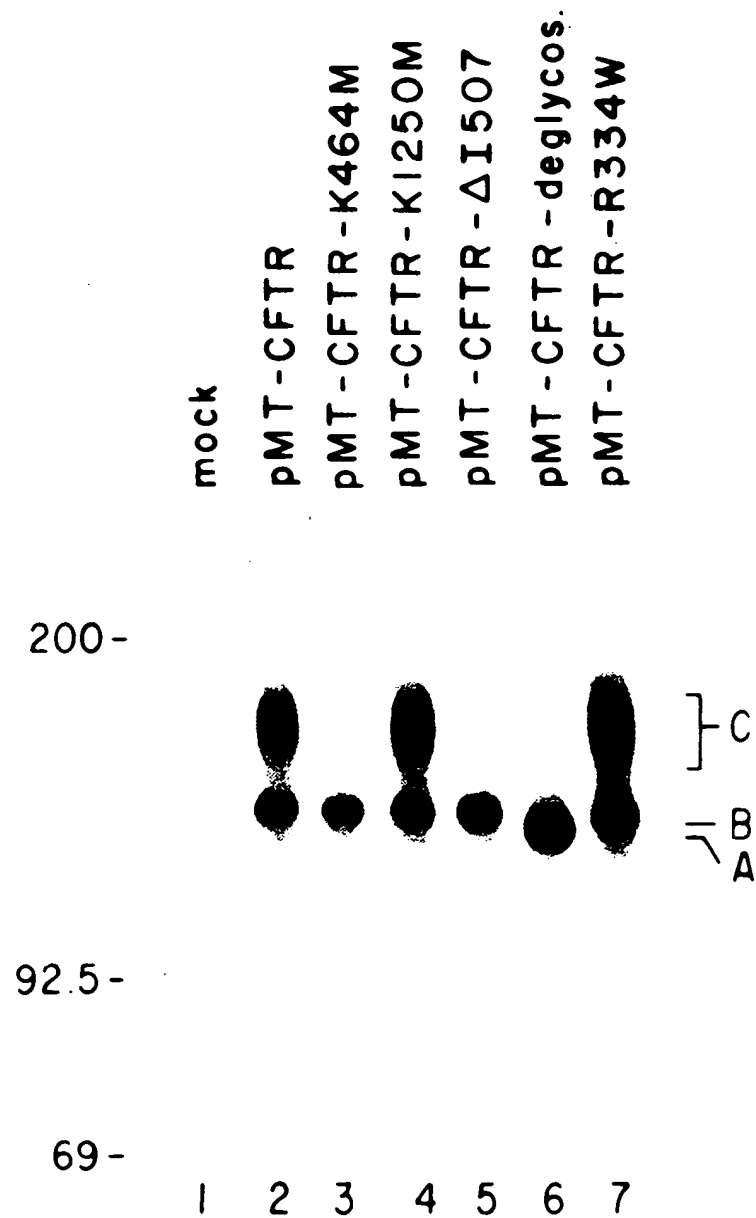


FIG.13

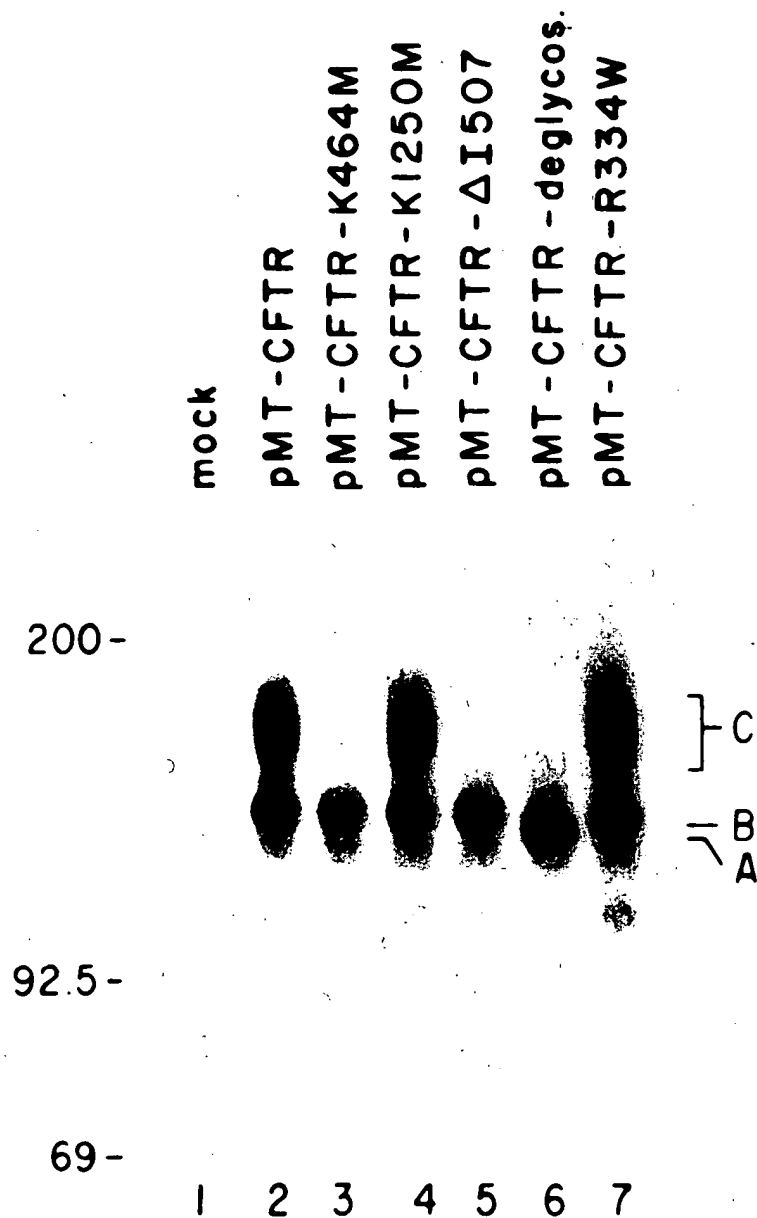


FIG.13

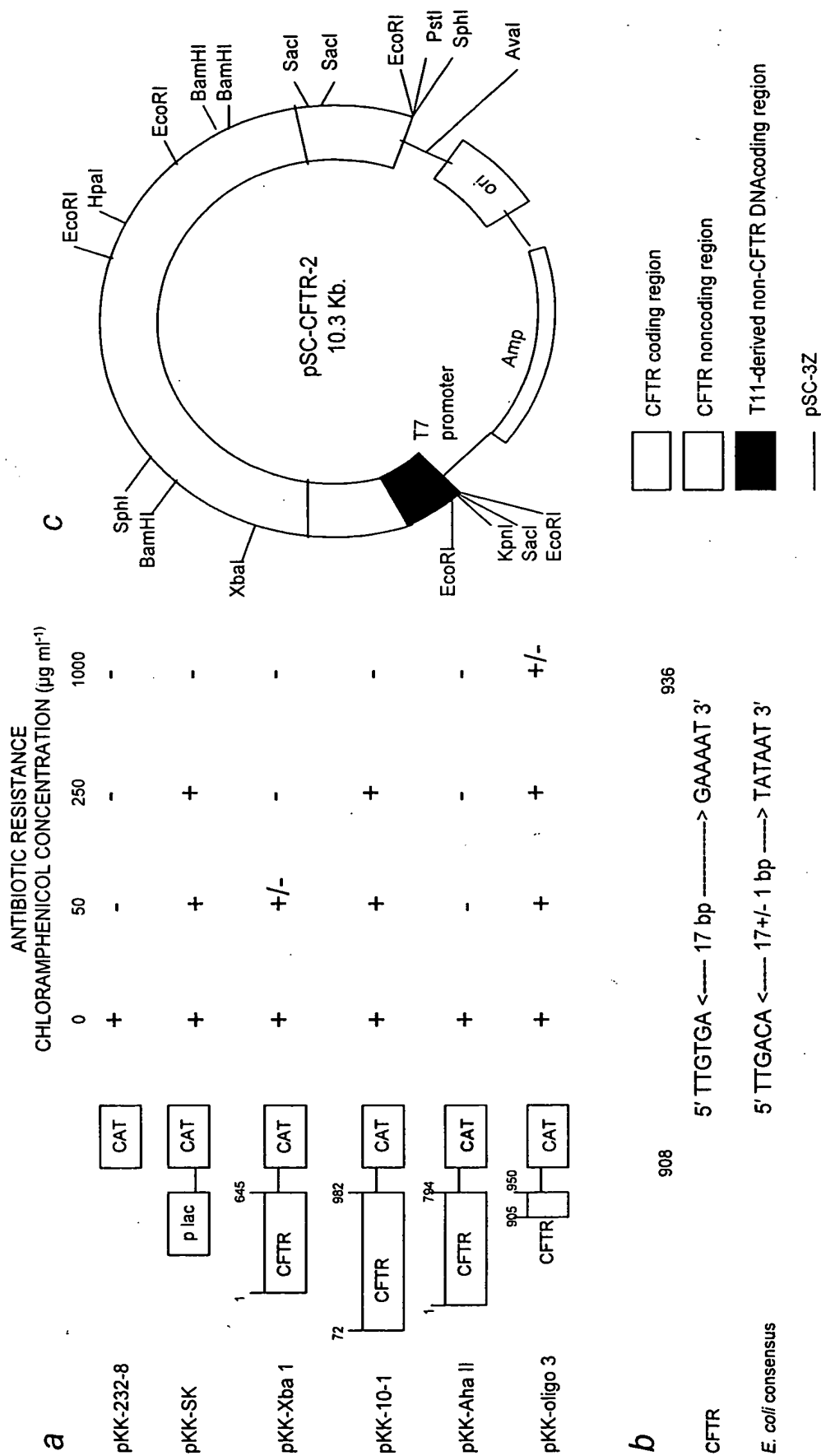


FIG. 14

1	AATTGGAAGCAAATGACATCACAGCAGGTCAGAGAAAAAGGG	42
43	TTGAGCGGCAGGCACCCAGAGTAGTAGGTCTTTGGCATTAGG	84
85	AGCTTGAGCCCAGACGGCCCTAGCAGGGACCCAGCGCCCGA	126
1	MetGlnArgSerProLeuGluLysAlaSerValVal	12
127	GAGACCATGCAGAGGTCGCCTCTGGAAAAGGCCAGCGTTGTC	168
13	SerLysLeuPhePheSerTrpThrArgProIleLeuArgLys	26
169	TCCAAACTTTTTTTCAGCTGGACCAGACCAATTTTGAGGAAA	210
27	GlyTyrArgGlnArgLeuGluLeuSerAspIleTyrGlnIle	40
211	GGATACAGACAGCGCCTGGAATTGTCAGACATATACCAAATC	252
41	ProSerValAspSerAlaAspAsnLeuSerGluLysLeuGlu	54
253	CCTTCTGTTGATTCTGCTGACAATCTATCTGAAAAATTGGAA	294
55	ArgGluTrpAspArgGluLeuAlaSerLysLysAsnProLys	68
295	AGAGAATGGGATAGAGAGCTGGCTTCAAAGAAAAATCCTAAA	336
69	LeuIleAsnAlaLeuArgArgCysPhePheTrpArgPheMet	82
337	CTCATTAATGCCCTTCGGCGATGTTTTTCTGGAGATTTATG	378
83	PheTyrGlyIlePheLeuTyrLeuGlyGluValThrLysAla	96
379	TTCTATGGAATCTTTTTATATTTAGGGGAAGTCACCAAAGCA	420
97	ValGlnProLeuLeuLeuGlyArgIleIleAlaSerTyrAsp	110
421	GTACAGCCTCTCTTACTGGGAAGAATCATAGCTTCCTATGAC	462
111	ProAspAsnLysGluGluArgSerIleAlaIleTyrLeuGly	124
463	CCGGATAACAAGGAGGAACGCTCTATCGCGATTTATCTAGGC	504
125	IleGlyLeuCysLeuLeuPheIleValArgThrLeuLeuLeu	138
505	ATAGGCTTATGCCTTCTCTTTATTGTGAGGACACTGCTCCTA	546
139	HisProAlaIlePheGlyLeuHisHisIleGlyMetGlnMet	152
547	CACCCAGCCATTTTTGGCCTTCATCACATTGGAATGCAGATG	588
153	ArgIleAlaMetPheSerLeuIleTyrLysLysThrLeuLys	166
589	AGAATAGCTATGTTTAGTTTGATTTATAAGAAGACTTTAAAG	630
167	LeuSerSerArgValLeuAspLysIleSerIleGlyGlnLeu	180
631	CTGTCAAGCCGTGTTCTAGATAAAATAAGTATTGGACAACCTT	672
181	ValSerLeuLeuSerAsnAsnLeuAsnLysPheAspGluGly	194
673	GTTAGTCTCCTTTCCAACAACCTGAACAAATTTGATGAAGGA	714

FIG. 15A

195	LeuAlaLeuAlaHisPheValTrpIleAlaProLeuGlnVal	208
715	CTTGCATTGGCACATTTTCGTGTGGATCGCTCCTTTGCAAGTG	756
209	AlaLeuLeuMetGlyLeuIleTrpGluLeuLeuGlnAlaSer	222
757	GCACTCCTCATGGGGCTAATCTGGGAGTTGTTACAGGCGTCT	798
223	AlaPheCysGlyLeuGlyPheLeuIleValLeuAlaLeuPhe	236
799	GCCTTCTGTGGACTTGGTTTCCTGATAGTCCTTGCCCTTTT	840
237	GlnAlaGlyLeuGlyArgMetMetMetLysTyrArgAspGln	250
841	CAGGCTGGGCTAGGGAGAATGATGATGAAGTACAGAGATCAG	882
251	ArgAlaGlyLysIleSerGluArgLeuValIleThrSerGlu	264
883	AGAGCTGGGAAGATCAGTGAAAGACTTGTGATTACCTCAGAA	924
265	MetIleGluAsnIleGlnSerValLysAlaTyrCysTrpGlu	278
925	ATGATTGAAAATATCCAATCTGTTAAGGCATACTGCTGGGAA	966
279	GluAlaMetGluLysMetIleGluAsnLeuArgGlnThrGlu	292
967	GAAGCAATGGAAAAAATGATTGAAAACCTAAGACAAACAGAA	1008
293	LeuLysLeuThrArgLysAlaAlaTyrValArgTyrPheAsn	306
1009	CTGAAACTGACTCGGAAGGCAGCCTATGTGAGATACTTCAAT	1050
307	SerSerAlaPhePhePheSerGlyPhePheValValPheLeu	320
1051	AGCTCAGCCTTCTTCTTCTCAGGGTTCTTTGTGGTGTTTT	1092
321	SerValLeuProTyrAlaLeuIleLysGlyIleIleLeuArg	334
1093	TCTGTGCTTCCCTATGCACTAATCAAAGGAATCATCCTCCGG	1134
335	LysIlePheThrThrIleSerPheCysIleValLeuArgMet	348
1135	AAAATATTCACCACCATCTCATTCTGCATTGTTCTGCGCATG	1176
349	AlaValThrArgGlnPheProTrpAlaValGlnThrTrpTyr	362
1177	GCGGTCACCTCGGCAATTTCCCTGGGCTGTACAAACATGGTAT	1218
363	AspSerLeuGlyAlaIleAsnLysIleGlnAspPheLeuGln	376
1219	GACTCTCTTGGAGCAATAAACAAAATACAGGATTTCTTACAA	1260
377	LysGlnGluTyrLysThrLeuGluTyrAsnLeuThrThrThr	390
1261	AAGCAAGAATATAAGACATTGGAATATACTTAACGACTACA	1302
391	GluValValMetGluAsnValThrAlaPheTrpGluGluGly	404
1303	GAAGTAGTGATGGAGAATGTAACAGCCTTCTGGGAGGAGGGA	1344
405	PheGlyGluLeuPheGluLysAlaLysGlnAsnAsnAsnAsn	418
1345	TTTGGGGAATTATTTGAGAAAGCAAACAAAACAATAACAAT	1386

FIG. 15B

419	ArgLysThrSerAsnGlyAspAspSerLeuPhePheSerAsn	432
1387	AGAAAACTTCTAATGGTGATGACAGCCTCTTCTTCAGTAAT	1428
433	PheSerLeuLeuGlyThrProValLeuLysAspIleAsnPhe	446
1429	TTCTCACTTCTTGGTACTCCTGTCCTGAAAGATATTAATTTC	1470
447	LysIleGluArgGlyGlnLeuLeuAlaValAlaGlySerThr	460
1471	AAGATAGAAAGAGGACAGTTGTTGGCGGTTGCTGGATCCACT	1512
461	GlyAlaGlyLysThrSerLeuLeuMetMetIleMetGlyGlu	474
1513	GGAGCAGGCAAGACTTCACTTCTAATGATGATTATGGGAGAA	1554
475	LeuGluProSerGluGlyLysIleLysHisSerGlyArgIle	488
1555	CTGGAGCCTTCAGAGGGTAAATTAAGCACAGTGGAAGAATT	1596
489	SerPheCysSerGlnPheSerTrpIleMetProGlyThrIle	502
1597	TCATTCTGTTCTCAGTTTTCTGGATTATGCCTGGCACCATT	1638
503	LysGluAsnIleIlePheGlyValSerTyrAspGluTyrArg	516
1639	AAAGAAAATATCATCTTTGGTGTTTCTATGATGAATATAGA	1680
517	TyrArgSerValIleLysAlaCysGlnLeuGluGluAspIle	530
1681	TACAGAAGCGTCATCAAAGCATGCCAACTAGAAGAGGACATC	1722
531	SerLysPheAlaGluLysAspAsnIleValLeuGlyGluGly	544
1723	TCCAAGTTTGCAGAGAAAGACAATATAGTTCTTGGAGAAGGT	1764
545	GlyIleThrLeuSerGlyGlyGlnArgAlaArgIleSerLeu	558
1765	GGAATCACACTGAGTGGAGGTCAACGAGCAAGAATTTCTTTA	1806
559	AlaArgAlaValTyrLysAspAlaAspLeuTyrLeuLeuAsp	572
1807	GCAAGAGCAGTATACAAAGATGCTGATTTGTATTTATTAGAC	1848
573	SerProPheGlyTyrLeuAspValLeuThrGluLysGluIle	586
1849	TCTCCTTTTGGATACCTAGATGTTTTAACAGAAAAAGAAATA	1890
587	PheGluSerCysValCysLysLeuMetAlaAsnLysThrArg	600
1891	TTTGAAAGCTGTGTCTGTAAACTGATGGCTAACAAAAGTAGG	1932
601	IleLeuValThrSerLysMetGluHisLeuLysLysAlaAsp	614
1933	ATTTTGGTCACTTCTAAATGGAACATTTAAAGAAAGCTGAC	1974
615	LysIleLeuIleLeuHisGluGlySerSerTyrPheTyrGly	628
1975	AAAATATTAATTTTGCATGAAGGTAGCAGCTATTTTTATGGG	2016
629	ThrPheSerGluLeuGlnAsnLeuGlnProAspPheSerSer	642
2017	ACATTTTCAGAACTCCAAATCTACAGCCAGACTTTAGCTCA	2058

FIG. 15C

643	LysLeuMetGlyCysAspSerPheAspGlnPheSerAlaGlu	656
2059	AAACTCATGGGATGTGATTCTTTCGACCAATTTAGTGCAGAA	2100
657	ArgArgAsnSerIleLeuThrGluThrLeuHisArgPheSer	670
2101	AGAAGAAATTCAATCCTAACTGAGACCTTACACCGTTTCTCA	2142
671	LeuGluGlyAspAlaProValSerTrpThrGluThrLysLys	684
2143	TTAGAAGGAGATGCTCCTGTCTCCTGGACAGAAACAAAAAA	2184
685	GlnSerPheLysGlnThrGlyGluPheGlyGluLysArgLys	698
2185	CAATCTTTTAAACAGACTGGAGAGTTTGGGGAAAAAAGGAAG	2226
699	AsnSerIleLeuAsnProIleAsnSerIleArgLysPheSer	712
2227	AATTCTATTCTCAATCCAATCAACTCTATACGAAAATTTTCC	2268
713	IleValGlnLysThrProLeuGlnMetAsnGlyIleGluGlu	726
2269	ATTGTGCAAAAGACTCCCTTACAAATGAATGGCATCGAAGAG	2310
727	AspSerAspGluProLeuGluArgArgLeuSerLeuValPro	740
2311	GATTCTGATGAGCCTTTAGAGAGAAGGCTGTCCTTAGTACCA	2352
741	AspSerGluGlnGlyGluAlaIleLeuProArgIleSerVal	754
2353	GATTCTGAGCAGGGAGAGGCGATACTGCCTCGCATCAGCGTG	2394
755	IleSerThrGlyProThrLeuGlnAlaArgArgArgGlnSer	768
2395	ATCAGCACTGGCCCCACGCTTCAGGCACGAAGGAGGCAGTCT	2436
769	ValLeuAsnLeuMetThrHisSerValAsnGlnGlyGlnAsn	782
2437	GTCCTGAACCTGATGACACACTCAGTTAACCAAGGTCAGAAC	2478
783	IleHisArgLysThrThrAlaSerThrArgLysValSerLeu	796
2479	ATTCACCGAAAGACAACAGCATCCACACGAAAAGTGTCACTG	2520
797	AlaProGlnAlaAsnLeuThrGluLeuAspIleTyrSerArg	810
2521	GCCCCTCAGGCAAACCTTGACTGAAGTGGATATATATTCAAGA	2562
811	ArgLeuSerGlnGluThrGlyLeuGluIleSerGluGluIle	824
2563	AGGTTATCTCAAGAACTGGCTTGGAAATAAGTGAAGAAATT	2604
825	AsnGluGluAspLeuLysGluCysLeuPheAspAspMetGlu	838
2605	AACGAAGAAGACTTAAAGGAGTGCCTTTTTTGATGATATGGAG	2646
839	SerIleProAlaValThrThrTrpAsnThrTyrLeuArgTyr	852
2647	AGCATACCAGCAGTGACTACATGGAACACATACCTTCGATAT	2688
853	IleThrValHisLysSerLeuIlePheValLeuIleTrpCys	866
2689	ATTACTGTCCACAAGAGCTTAATTTTTGTGCTAATTTGGTGC	2730

FIG. 15D

867	LeuValIlePheLeuAlaGluValAlaAlaSerLeuValVal	880
2731	TTAGTAATTTTTCTGGCAGAGGTGGCTGCTTCTTTGGTTGTG	2772
881	LeuTrpLeuLeuGlyAsnThrProLeuGlnAspLysGlyAsn	894
2773	CTGTGGCTCCTTGGAAACACTCCTCTTCAAGACAAAGGGAAT	2814
895	SerThrHisSerArgAsnAsnSerTyrAlaValIleIleThr	908
2815	AGTACTCATAGTAGAAATAACAGCTATGCAGTGATTATCACC	2856
909	SerThrSerSerTyrTyrValPheTyrIleTyrValGlyVal	922
2857	AGCACCAGTTCGTATTATGTGTTTTACATTTACGTGGGAGTA	2898
923	AlaAspThrLeuLeuAlaMetGlyPhePheArgGlyLeuPro	936
2899	GCCGACACTTTGCTTGCTATGGGATTCTTCAGAGGTCTACCA	2940
937	LeuValHisThrLeuIleThrValSerLysIleLeuHisHis	950
2941	CTGGTGCATACTCTAATCACAGTGTGCGAAAATTTTACACCAC	2982
951	LysMetLeuHisSerValLeuGlnAlaProMetSerThrLeu	964
2983	AAAATGTTACATTCTGTTCTTCAAGCACCTATGTCAACCCTC	3024
965	AsnThrLeuLysAlaGlyGlyIleLeuAsnArgPheSerLys	978
3025	AACACGTTGAAAGCAGGTGGGATTCTTAATAGATTCTCCAAA	3066
979	AspIleAlaIleLeuAspAspLeuLeuProLeuThrIlePhe	992
3067	GATATAGCAATTTTGGATGACCTTCTGCCTCTTACCATATTT	3108
993	AspPheIleGlnLeuLeuLeuIleValIleGlyAlaIleAla	1006
3109	GACTTCATCCAGTTGTTATTAATTGTGATTGGAGCTATAGCA	3150
1007	ValValAlaValLeuGlnProTyrIlePheValAlaThrVal	1020
3151	GTTGTGCGCAGTTTTACAACCCTACATCTTTGTTGCAACAGTG	3192
1021	ProValIleValAlaPheIleMetLeuArgAlaTyrPheLeu	1034
3193	CCAGTGATAGTGGCTTTTATTATGTTGAGAGCATATTTCTC	3234
1035	GlnThrSerGlnGlnLeuLysGlnLeuGluSerGluGlyArg	1048
3235	CAAACCTCACAGCAACTCAAACAACCTGGAATCTGAAGGCAGG	3276
1049	SerProIlePheThrHisLeuValThrSerLeuLysGlyLeu	1062
3277	AGTCCAATTTTCACTCATCTTGTTACAAGCTTAAAAGGACTA	3318
1063	TrpThrLeuArgAlaPheGlyArgGlnProTyrPheGluThr	1076
3319	TGGACACTTCGTGCCTTCGGACGGCAGCCTTACTTTGAAACT	3360
1077	LeuPheHisLysAlaLeuAsnLeuHisThrAlaAsnTrpPhe	1090
3361	CTGTTCCACAAAGCTCTGAATTTACATACTGCCAACTGGTTC	3402

FIG. 15E

1091	LeuTyrLeuSerThrLeuArgTrpPheGlnMetArgIleGlu	1104
3403	TTGTACCTGTCAACACTGCGCTGGTTCCAAATGAGAATAGAA	3444
1105	MetIlePheValIlePhePheIleAlaValThrPheIleSer	1118
3445	ATGATTTTTGTTCATCTTCTTCATTGCTGTTACCTTCATTTCC	3486
1119	IleLeuThrThrGlyGluGlyGluGlyArgValGlyIleIle	1132
3487	ATTTTAACAACAGGAGAAGGAGAAGGAAGAGTTGGTATTATC	3528
1133	LeuThrLeuAlaMetAsnIleMetSerThrLeuGlnTrpAla	1146
3529	CTGACTTTAGCCATGAATATCATGAGTACATTGCAGTGGGCT	3570
1147	ValAsnSerSerIleAspValAspSerLeuMetArgSerVal	1160
3571	GTAAACTCCAGCATAGATGTGGATAGCTTGATGCGATCTGTG	3612
1161	SerArgValPheLysPheIleAspMetProThrGluGlyLys	1174
3613	AGCCGAGTCTTTAAGTTCATTGACATGCCAACAGAAGGTAAA	3654
1175	ProThrLysSerThrLysProTyrLysAsnGlyGlnLeuSer	1188
3655	CCTACCAAGTCAACCAACCATAACAAGAATGGCCAACTCTCG	3696
1189	LysValMetIleIleGluAsnSerHisValLysLysAspAsp	1202
3697	AAAGTTATGATTATTGAGAATTCACACGTGAAGAAAGATGAC	3738
1203	IleTrpProSerGlyGlyGlnMetThrValLysAspLeuThr	1216
3739	ATCTGGCCCTCAGGGGGCCAAATGACTGTCAAAGATCTCACA	3780
1217	AlaLysTyrThrGluGlyGlyAsnAlaIleLeuGluAsnIle	1230
3781	GCAAATACACAGAAGGTGGAAATGCCATATTAGAGAACATT	3822
1231	SerPheSerIleSerProGlyGlnArgValGlyLeuLeuGly	1244
3823	TCCTTCTCAATAAGTCCTGGCCAGAGGGTGGGCCTCTTGGGA	3864
1245	ArgThrGlySerGlyLysSerThrLeuLeuSerAlaPheLeu	1258
3865	AGAACTGGATCAGGGAAGAGTACTTTGTTATCAGCTTTTTTGTG	3906
1259	ArgLeuLeuAsnThrGluGlyGluIleGlnIleAspGlyVal	1272
3907	AGACTACTGAACACTGAAGGAGAAATCCAGATCGATGGTGTG	3948
1273	SerTrpAspSerIleThrLeuGlnGlnTrpArgLysAlaPhe	1286
3949	TCTTGGGATTCAATAACTTTGCAACAGTGGAGGAAAGCCTTT	3990
1287	GlyValIleProGlnLysValPheIlePheSerGlyThrPhe	1300
3991	GGAGTGATACCACAGAAAGTATTTATTTTTTCTGGAACATTT	4032
1301	ArgLysAsnLeuAspProTyrGluGlnTrpSerAspGlnGlu	1314
4033	AGAAAAAACTTGATCCCTATGAACAGTGGAGTGATCAAGAA	4074

FIG. 15F

1315	IleTrpLysValAlaAspGluValGlyLeuArgSerValIle	1328
4075	ATATGGAAAGTTGCAGATGAGGTTGGGCTCAGATCTGTGATA	4116
1329	GluGlnPheProGlyLysLeuAspPheValLeuValAspGly	1342
4117	GAACAGTTTCCTGGGAAGCTTGACTTTGTCCTTGTGGATGGG	4158
1343	GlyCysValLeuSerHisGlyHisLysGlnLeuMetCysLeu	1356
4159	GGCTGTGTCCTAAGCCATGGCCACAAGCAGTTGATGTGCTTG	4200
1357	AlaArgSerValLeuSerLysAlaLysIleLeuLeuLeuAsp	1370
4201	GCTAGATCTGTTCTCAGTAAGGCGAAGATCTTGCTGCTTGAT	4242
1371	GluProSerAlaHisLeuAspProValThrTyrGlnIleIle	1384
4243	GAACCCAGTGCTCATTGATCCAGTAACATACCAAATAATT	4284
1385	ArgArgThrLeuLysGlnAlaPheAlaAspCysThrValIle	1398
4285	AGAAGAACTCTAAACAAGCATTTGCTGATTGCACAGTAATT	4326
1399	LeuCysGluHisArgIleGluAlaMetLeuGluCysGlnGln	1412
4327	CTCTGTGAACACAGGATAGAAGCAATGCTGGAATGCCAACAA	4368
1413	PheLeuValIleGluGluAsnLysValArgGlnTyrAspSer	1426
4369	TTTTTGGTCATAGAAGAGAACAAAGTGCGGCAGTACGATTCC	4410
1427	IleGlnLysLeuLeuAsnGluArgSerLeuPheArgGlnAla	1440
4411	ATCCAGAAACTGCTGAACGAGAGGAGCCTCTTCCGGCAAGCC	4452
1441	IleSerProSerAspArgValLysLeuPheProHisArgAsn	1454
4453	ATCAGCCCCCTCCGACAGGGTGAAGCTCTTTCCCCACCGGAAC	4494
1455	SerSerLysCysLysSerLysProGlnIleAlaAlaLeuLys	1468
4495	TCAAGCAAGTGCAAGTCTAAGCCCCAGATTGCTGCTCTGAAA	4536
1469	GluGluThrGluGluGluValGlnAspThrArgLeuEnd	1482
4537	GAGGAGACAGAAGAAGAGGTGCAAGATACAAGGCTTTAGAGA	4578
4579	GCAGCATAAATGTTGACATGGGACATTTGCTCATGGAATTGG	4620
4621	AGCTCGTGGGACAGTCACCTCATGGAATTGGAGCTCGTGGA	4662
4663	CAGTTACCTCTGCCTCAGAAAACAAGGATGAATTAAGTTTTT	4704
4705	TTTTAAAAAAGAAACATTTGGTAAGGGGAATTGAGGACACTG	4746
4747	ATATGGGTCTTGATAAATGGCTTCCTGGCAATAGTCAAATTG	4788
4789	TGTGAAAGGTACTTCAAATCCTTGAAGATTTACCACTTGTGT	4830
4831	TTTGCAAGCCAGATTTTCCTGAAAACCTTGCCATGTGCTAG	4872
4873	TAATTGGAAAGGCAGCTCTAAA	4894

FIG. 15G